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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES • National Institutes of Health • National Institute on Alcohol Abuse and Alcoholism

FEATURE

NEW PREVALENCE ESTIMATES OF FETAL ALCOHOL SPECTRUM DISORDERS RANGE FROM 1 TO 5 PERCENT IN U.S. COMMUNITIES

Findings reflect a more comprehensive approach and larger sample size than previous studies



A study of more than 6,000 first-graders across 4 U.S. communities has found that a significant number of children have fetal alcohol spectrum disorders (FASD), with conservative rates ranging from 1 to 5 percent in community samples. The new findings represent more accurate prevalence estimates of FASD than prior research. Previous FASD estimates were based on smaller study populations and did not reflect the overall U.S. population.

The term FASD represents a range of health effects caused by prenatal alcohol exposure. Individuals with FASD may experience growth deficiencies, facial abnormalities, and organ damage, including to the brain. The effects of prenatal alcohol exposure on the brain can result in deficits that contribute to physical, cognitive, behavioral, and social challenges throughout life.

“Prenatal alcohol exposure is a leading preventable cause of developmental

disabilities worldwide,” says NIAAA Director George F. Koob, Ph.D. “Estimating the prevalence of FASD in the United States has been complex due to the challenges in identifying prenatally exposed children. The findings of this study confirm that FASD is a significant public health problem, and strategies to expand screening, diagnosis, prevention, and treatment are needed to address it.”

The study was conducted by the Collaboration on FASD Prevalence (CoFASP) consortium, which studies the prevalence of FASD among U.S. schoolchildren. Before the study began, consortium members established standardized classification criteria for FASD based on facial features, growth, and neurodevelopmental performance. The findings from the study, which was led by Philip May, Ph.D., of the University of North Carolina at Chapel Hill’s Nutrition Research Institute in Kannapolis, and Christina Chambers, Ph.D., of the University of California San Diego School of Medicine, were reported in *JAMA* in February.

Researchers collected data between 2010 and 2016 on 6,639 children in 4 communities from the U.S. Midwest, Rocky Mountain, Southeast, and Pacific Southwest regions. The sites were

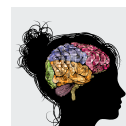
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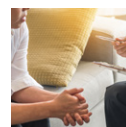


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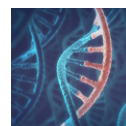
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FEATURE

BRAIN STUDIES POINT TO PERILS OF ADOLESCENT ALCOHOL USE



The brain takes longer to develop and mature than any other organ in the body. Beginning in the third week of gestation and extending into the mid-20s, an ongoing interplay of genetic and environmental factors results in the mature human brain, a structure composed of more than 100 billion neurons. Some of the most rapid and pronounced changes in the brain take place during childhood and adolescence.

During normal adolescent brain development, widespread structural and functional changes occur rapidly within individual brain regions and in the connections between them. These changes help the brain systems that regulate cognitive, emotional, and social behavior to mature. The extent and complexity of these changes make the adolescent brain particularly vulnerable to the adverse effects of alcohol. Indeed, studies have associated heavy alcohol use during adolescence with harm to various brain structures, lingering problems with cognitive functions such as attention and memory, and an increased risk for future alcohol use disorder (AUD) and other mental health disorders.

“We have long known that adolescent alcohol use is associated with many adverse outcomes, both during adolescence and in later life,” says

NIAAA Director George F. Koob, Ph.D. “Our expanding research investment in this area is allowing us to define more precisely why alcohol and the adolescent brain are a particularly dangerous combination.”

The brain is a highly complex organ. Human brain imaging studies have shown that, over the course of adolescence, the volume of gray matter—which represents the cell bodies of neurons and their connections with nearby neurons—decreases in the prefrontal cortex. This decrease likely reflects the normal process of “synaptic pruning,” through which the brain gets rid of excess connections that are no longer needed. However, the volume of white matter—which is important for pathways connecting neurons located at farther distances from each other—increases during adolescence, presumably reflecting enhanced brain connectivity and improved communication between areas. Initial findings from NIAAA-supported research indicate that adolescents who drink heavily, when compared with nondrinking adolescents, have accelerated reductions in gray matter and smaller increases in white matter.

To build on these findings, NIAAA supports the National Consortium on Alcohol and Neurodevelopment in Adolescence (NCANDA), a nationally representative, accelerated, longitudinal study of more than 800 youth. NCANDA’s accelerated design allows researchers to follow multiple youth cohorts, each starting at a different age, so that the cohorts together span a broader age range of interest than a traditional cohort design. The goals of the NCANDA study are to determine the short- and long-term effects of alcohol use on the developing adolescent brain and identify brain characteristics that predict AUD.

NIAAA, along with the National Institute on Drug Abuse, is a major contributor to the National Institutes

of Health Adolescent Brain Cognitive Development (ABCD) Study, a 10-year longitudinal study of 10,000 youth, the largest long-term study of brain development and child health in the United States. NCANDA and ABCD investigators are providing much-needed information about the neurodevelopmental consequences of alcohol and other drugs, alone and in combination.

A recent NCANDA study led by Adolf Pfefferbaum, M.D., of SRI International in Menlo Park, California, and colleagues found disordered brain growth trajectories among young people who initiated drinking during adolescence. The researchers noted possible factors that contribute to the abnormal trajectories include peak alcohol consumption in the past year and having a family history of AUD.

Another recent NCANDA investigation led by Eva Müller-Oehring, Ph.D., also of SRI International, and colleagues found that development of intrinsic functional networks (IFNs)—brain circuits that underlie specific functions—were susceptible to adolescent alcohol use. In particular, they reported evidence that IFNs associated with cognitive and emotional functioning become rewired among adolescents who exceeded the study’s criteria for no or low alcohol use. This effect, they conclude, may impede maturation of complex social and emotional behaviors.

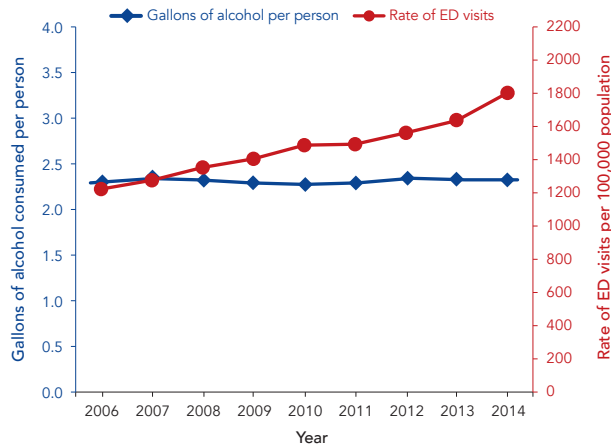
The growing evidence of alcohol’s impact on adolescent brain development, as well as its position as the substance of choice for young people, underscores the need for health professionals to screen adolescents for alcohol.

A 2016 study funded by NIAAA demonstrated that a single screening question about drinking frequency in the past year could help doctors identify adolescents at risk for alcohol problems. The study supported the use

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BY THE NUMBERS

U.S. Alcohol Consumption and Emergency Department (ED) Visits, 2006–2014



Source: Adapted from White et al., 2018.

ALCOHOL-RELATED EMERGENCY DEPARTMENT VISITS ON THE RISE

Alcohol misuse can be hazardous to your health, a fact spotlighted by a new study of U.S. emergency department (ED) visits. According to NIAAA researcher Aaron M. White, Ph.D., the study's lead author, the data suggest that the rise in the rate of ED visits appears related to an increase in the intensity of alcohol use among women and older adults who drink. (For more information, see the News From the Field story "Steep Increase in Rate of Alcohol-Related Emergency Department Visits.")

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selected to be more reflective of U.S. community populations than previous studies. At each site, first-graders in public and private schools were recruited across two academic years and evaluated based on the FASD criteria. Prenatal alcohol exposure was assessed by interviewing mothers or other close relatives.

The researchers found that the prevalence estimates for FASD among the selected sites ranged from 1.1 to 5 percent. This was the most conservative estimate and assumed no additional cases of FASD would be found in first-graders who did not participate in the study. When the researchers used a "weighted prevalence," an estimate that accounts for those who were eligible but did not participate in the study, the estimated prevalence of FASD was higher—ranging from 3.1 to 9.8 percent among the study sites. Of the 222 children diagnosed with FASD in the study, only 2 had been previously diagnosed with FASD, although many parents and guardians were aware of the children's learning and behavioral challenges. This finding suggests that children with FASD often go undiagnosed or misdiagnosed.

"We believe our study is the first to use school-based assessments, a common

methodology and classification system, and expert in-person evaluations for the full range of FASD on many children from communities across the United States," says Dr. May.

"This comprehensive approach should reflect estimates that more closely resemble the prevalence of FASD in the United States, and further highlights the public health burden of FASD," adds Dr. Chambers.

Estimating the prevalence of FASD is challenging, in part, because FASD can be difficult to distinguish from other developmental disorders that share certain learning and behavioral deficits. Also, individuals can have FASD without the hallmark facial features of fetal alcohol syndrome.

Most previous studies of FASD prevalence in the United States have been conducted using surveillance or clinic-based studies, which misses undiagnosed cases of FASD and leads to underestimates. Studies have also been conducted among high-risk populations, which results in prevalence rates that cannot be generalized to the population as a whole.

The previously accepted FASD estimate of 1 percent of U.S. children resulted from clinic-based studies and studies of single communities,

which assessed small samples among selected populations.

"Because of the hidden nature of the disabilities, some have continued to believe that FASD is a rare disorder, or they question its prevalence," says Tom Donaldson, President of the National Organization on Fetal Alcohol Syndrome (NOFAS).

"I would say this research truly once and for all firmly established the magnitude of FASD. It's now really time for us to push forward and make this study the catalyst for change and progress."

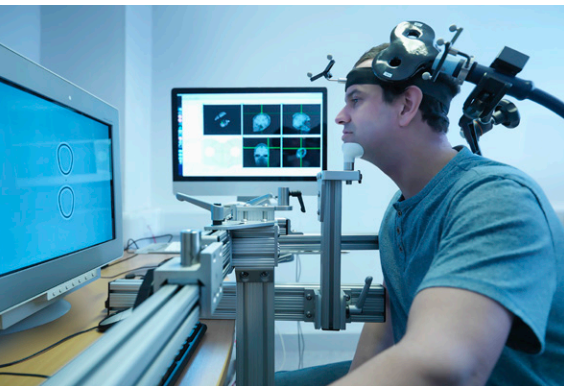
Soon after the findings were published in *JAMA*, the lead study authors, NIAAA experts, and FASD advocates came together to discuss the significance of the study. A recording of the teleconference is available at: <https://www.niaaa.nih.gov/news-events/news-noteworthy/teleconference-prevalence-fetal-alcohol-spectrum-disorders-among-us>.

Reference:

May, P.A.; Chambers, C.D.; Kalberg, W.O.; Zellner, J.; Feldman, H.; Buckley, D.; et al. Prevalence of fetal alcohol spectrum disorders in 4 U.S. communities. *JAMA* 319(5):474–482, 2018. PMID: 29411031

NEWS FROM THE FIELD

REHABILITATING THE ADDICTED BRAIN WITH TRANSCRANIAL MAGNETIC STIMULATION



Recent studies have highlighted the potential of transcranial magnetic stimulation (TMS) as an innovative, safe, and cost-effective treatment for alcohol and other substance use disorders. A new review article by Antonello Bonci, M.D., of the National Institute on Drug Abuse (NIDA), with Lorenzo Leggio, M.D., Ph.D., of NIAAA, and colleagues in the United States and Italy, addresses the scientific rationale for using repetitive TMS (rTMS) to treat patients with addictive disorders. Drawing on data from studies in animals and preliminary research in humans, the review suggests that rTMS of frontal brain regions may change specific brain circuits and lead to substantial changes in addictive behaviors.

TMS is a noninvasive method for delivering electric field pulses into the brain. The procedure involves holding a magnetic coil over the scalp so magnetic fields can efficiently pass through the skull, allowing strong currents into the underlying brain tissue. TMS can be used to either increase or decrease neuronal firing in targeted brain areas.

Delivering many TMS pulses in sequences can cause long-term brain changes that facilitate or impede the excitability of neurons. It is not completely understood how TMS induces these long-term neurophysiological changes. Although TMS is a relatively new approach to treating alcohol and other substance use disorders, it is currently an approved therapy for treatment-resistant depression.

Researchers have hypothesized that administering TMS can alleviate cocaine use disorder by strengthening activity in the dorsolateral prefrontal cortex (DLPFC), an area that regulates impulse control, and brain regions that receive input from the DLPFC.

Rodent studies have supported this hypothesis. Rats that compulsively sought cocaine stopped doing so when researchers experimentally increased

activity levels in the prefrontal cortex, a subregion of the rat cortex that seems to share some functional similarities with the human DLPFC.

Human studies have yielded promising results for TMS as well. In pilot studies, patients who received TMS were more likely to abstain from cocaine than patients who received medications solely for symptoms associated with abstinence.

The review authors reported that TMS appears ready to be subjected to large, randomized controlled trials to test this promising approach to treating alcohol and other substance use disorders. They conclude, “Its mechanisms of action, which tap into the brain’s strong potential for functional reorganization, offer new hope for creating enduring changes to enable the rewiring of a brain system gone awry.”

Reference:

Diana, M.; Raj, T.; Melis, M.; Nummenmaa, A.; Leggio, L.; and Bonci, A. Rehabilitating the addicted brain with transcranial magnetic stimulation. *Nature Reviews: Neuroscience* 18(11):685–693, 2017. PMID: 28951609

NEWS FROM THE FIELD

BEHAVIORAL INTERVENTIONS THAT ADDRESS ALCOHOL USE HELP PEOPLE LIVING WITH HIV/AIDS



There are more than 36 million people living with HIV/AIDS (PLWHA) worldwide. Alcohol misuse is a significant concern for this population because it contributes to risky sexual behavior, reduces adherence to HIV medication regimens, and exacerbates other health conditions. Interventions that address alcohol misuse among PLWHA have the potential to help improve their health outcomes.

A systematic review and meta-analysis led by Lori Scott-Sheldon, Ph.D., at the Centers for Behavioral and Preventive Medicine at The Miriam Hospital and the Department of Psychiatry and Human Behavior at Brown University, both in Providence, Rhode Island, evaluated the efficacy of existing behavioral interventions in reducing alcohol use among PLWHA.

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NEWS FROM THE FIELD

MICRORNAs MAY HAVE THERAPEUTIC POTENTIAL FOR ALCOHOL-INDUCED LIVER INJURY



MicroRNAs, or miRNAs, are short strands of RNA that play important roles in gene regulation. In two recent studies, NIAAA-supported researchers identified two miRNAs that may help protect against alcohol-induced liver injury. Paramananda Saikia, Ph.D., and colleagues at the Cleveland Clinic, in studies conducted in mice, demonstrated that levels of a specific miRNA called miR181b-3p decreased in Kupffer cells in response to ethanol treatment. Previous research has shown that increased inflammatory signaling by Kupffer cells contributes to alcohol-associated liver disease (AALD).

Studies have suggested that the anti-inflammatory agent hyaluronic acid (HA35) could have protective effects on the liver during ethanol exposure, and in the present study, HA35 had an anti-inflammatory effect on Kupffer cells and prevented the decrease in miR181b-3p. These findings suggest that miR181b-3p may be part of an inflammatory-signaling pathway with therapeutic potential for the treatment of AALD.

In another study, Abhishek Satishchandran, M.D./Ph.D. Candidate, Gyongyi Szabo, M.D., Ph.D., and a team of researchers at the University of Massachusetts Medical School in Worcester observed a reduction of miR122 in the livers of people with AALD, as well as in alcohol-fed mice. The most abundant liver miRNA, miR122, has been implicated in controlling fatty acid and cholesterol metabolism. By increasing miR122 expression therapeutically in mice, the

researchers were able to reduce alcohol-induced liver injury, whereas injections of molecules that block miR122 increased signs of liver damage. The researchers suggest that these miR122-related mechanisms could potentially be manipulated to reduce the severity of AALD in humans.

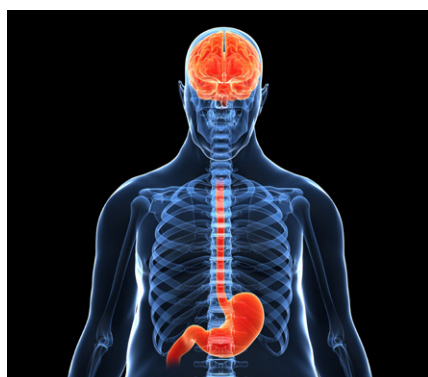
References:

Saikia, P.; Bellos, D.; McMullen, M.R.; Pollard, K.A.; de la Motte, C.; and Nagy, L.E. MicroRNA 181b-3p and its target importin $\alpha 5$ regulate toll-like receptor 4 signaling in Kupffer cells and liver injury in mice in response to ethanol. *Hepatology* 66(2):602–615, 2017. PMID: 28257601

Satishchandran, A.; Ambade, A.; Rao, S.; Hsueh, Y.C.; Iracheta-Vellve, A.; Tornai, D.; Lowe, P.; Gyongyosi, B.; Li, J.; Catalano, D.; Zhong, L.; Kody, K.; Xie, J.; Bala, S.; Gao, G.; and Szabo, G. MicroRNA 122, regulated by GRLH2, protects livers of mice and patients from ethanol-induced liver disease. *Gastroenterology* 154(1):238–252.e7, 2018. PMID: 28987423

NEWS FROM THE FIELD

HUNGER HORMONE AFFECTS ALCOHOL INTAKE



A new study by NIAAA researchers provides further evidence that a hormone produced in the stomach influences alcohol consumption in humans. As reported in *Molecular Psychiatry*, researchers led by Lorenzo

Leggio, M.D., Ph.D., demonstrated that the hormone, called ghrelin, may be a promising target for developing new medications for alcohol use disorder (AUD).

Dr. Leggio, Chief of the Section on Clinical Psychoneuroendocrinology and Neuropsychopharmacology, an NIAAA intramural laboratory jointly funded with the National Institute on Drug Abuse, noted that preclinical studies have shown that ghrelin has complex interactions with the brain, including the brain's reward and stress pathways. Ghrelin is known mostly for its role in regulating appetite and is often called the "hunger" hormone.

"While studies in animals have pointed to ghrelin's possible role in alcohol-

seeking behavior, its impact on alcohol intake by humans has been unclear," says Dr. Leggio.

In the current study, Dr. Leggio and his colleagues conducted a randomized, placebo-controlled study of humans who were heavy drinkers with AUD. Mehdi Farokhnia, M.D., a Postdoctoral Fellow in Dr. Leggio's intramural laboratory, is the first author of the study.

In the study, participants received either ghrelin or placebo, intravenously. In one experiment, the participants could press a button to receive an intravenous infusion of alcohol during the ghrelin or placebo session. The researchers found that ghrelin, compared to placebo,

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NEWS FROM THE FIELD

STEEP INCREASE IN RATE OF ALCOHOL-RELATED EMERGENCY DEPARTMENT VISITS



The rate of alcohol-related visits to U.S. emergency departments (EDs) increased by nearly 50 percent between 2006 and 2014, especially among females and drinkers who are middle-aged or older, according to a new study conducted by NIAAA researchers.

“In just 9 years, the number of people transported to the ED annually for medical emergencies caused or exacerbated by alcohol increased from about 3 million to 5 million,” says NIAAA Director George F. Koob, Ph.D. “These findings are indicative of the detrimental effects that acute and chronic alcohol misuse have on public health, and the significant burden they place on our health care system.”

As reported in *Alcoholism: Clinical and Experimental Research*, researchers led by Aaron M. White, Ph.D., Senior Scientific Advisor to the NIAAA Director, analyzed data from the Nationwide Emergency Department Sample (NEDS), the largest ED database in the United States. The research team assessed trends in ED visits that involved acute and chronic alcohol consumption among individuals 12 and older.

In the study, ED visits related to acute alcohol consumption were classified by standard diagnostic codes associated with alcohol misuse over a short period of time, such as acute alcohol intoxication and accidental alcohol poisoning, while visits involving chronic alcohol misuse were identified by diagnostic codes for conditions associated with long-term drinking, such as alcohol withdrawal and alcohol-related cirrhosis of the liver.

The rate of all alcohol-related ED visits increased 47 percent between 2006 and 2014, which translates to an average annual increase of 210,000 alcohol-related ED visits. The rate of visits for acute alcohol consumption rose by 40 percent, and the rate of visits related to chronic alcohol consumption increased 58 percent. The NEDS data also showed

that total annual costs of alcohol-related visits increased from \$4.1 billion to \$15.3 billion during this time.

Although men account for more alcohol-related ED visits than women, the rate of such visits increased more among females than males (5.3 percent versus 4.0 percent, annually). This increase was driven primarily by a larger increase in the rate of chronic alcohol misuse-related visits for females than males (6.9 percent versus 4.5 percent, annually).

“Recent studies suggest that the drinking habits of females and males are becoming more similar in the United States,” says Dr. White. “The larger increase in the rate of ED visits among females compared to males provides further evidence of narrowing gender gaps in alcohol use and related harms.”

Reference:

White, A.M.; Slater, M.E.; Ng, G.; Hingson, R.; and Breslow, R. Trends in alcohol-related emergency department visits in the United States: Results from the Nationwide Emergency Department Sample, 2006 to 2014. *Alcoholism: Clinical and Experimental Research* 42(2):352–359, 2018. PMID: 29293274

FEATURE: Brain Studies Point to Perils . . . Continued from page 2

of the age-based screening thresholds put forward in NIAAA’s Alcohol Screening and Brief Intervention for Youth: A Practitioner’s Guide

and demonstrated that simple screening tools, such as those in NIAAA’s Youth Guide, are efficient and effective. The Youth Guide is

available at: <https://www.niaaa.nih.gov/publications/clinical-guides-and-manuals/alcohol-screening-and-brief-intervention-youth>.

References:

Pfefferbaum, A.; Kwon, D.; Brumback, T.; Thompson, W.K.; Cummins, K.; Tapert, S.F.; Brown, S.A.; Colrain, I.M.; Baker, F.C.; Prouty, D.; De Bellis, M.D.; Clark, D.B.; Nagel, B.J.; Chu, W.; Park, S.H.; Pohl, K.M.; and Sullivan, E.V. Altered brain developmental trajectories in adolescents after initiating drinking. *American Journal of Psychiatry* 175(4):370–380, 2018. PMID: 29084454

Müller-Oehring, E.M.; Kwon, D.; Nagel, B.J.; Sullivan, E.V.; Chu, W.; Rohlfing, T.; Prouty, D.; Nichols, B.N.; Poline, J.B.; Tapert, S.F.; Brown, S.A.; Cummins, K.; Brumback, T.; Colrain, I.M.; Baker, F.C.; De Bellis, M.D.; Voyvodic, J.T.; Clark, D.B.; Pfefferbaum, A.; and Pohl, K.M. Influences of age, sex, and moderate alcohol drinking on the intrinsic functional architecture of adolescent brains. *Cerebral Cortex* 28(3):1049–1063, 2018. PMID: 28168274

Clark, D.B.; Martin, C.S.; Chung, T.; Gordon, A.J.; Fiorentino, L.; Tootell, M.; and Rubio, D.M. Screening for underage drinking and DSM-5 alcohol use disorder in rural primary care practice. *Journal of Pediatrics* 173:214–220, 2016. PMID: 27059911

5 QUESTIONS WITH . . .

LORENZO LEGGIO, M.D., PH.D.

Chief of the NIAAA/NIDA Section on Clinical Psychoneuroendocrinology and Neuropsychopharmacology



1 You are the Chief of the Section on Clinical Psychoneuroendocrinology and Neuropsychopharmacology, a joint NIAAA and National Institute on Drug Abuse (NIDA) laboratory. What are the objectives of this lab?

When I moved to the NIH, I was asked to name my lab. I initially said, “Addiction Medicine,” but I was told that in the IRP [Intramural Research Program], labs’ names typically reflect their focus and vision. So, I came up with a name that turned out to be a tongue twister. **Clinical** because we conduct human research, mostly with individuals with AUD [alcohol use disorder]; however, we are also taking advantage of the IRP environment to build translational collaborative projects with preclinical labs.

Psychoneuroendocrinology because we study appetitive hormones (ghrelin, oxytocin, GLP-1, leptin, just to name a few) potentially relevant for AUD with a special interest in understanding how they work in the context of the microbiome-gut-liver-brain axis and how this information may shed light on the mechanisms underlying the development and maintenance of AUD.

Neuropsychopharmacology because our ultimate goal is to use information related to the microbiome-gut-liver-brain axis toward the development of new treatments for AUD.

2 A unique feature of your lab is the re-creation of an actual “bar” inside the NIH Clinical Center. Why did you create this bar lab?

Before moving to NIAAA/NIDA, I was PI [Principal Investigator] at Brown University, where we had created a simpler version of the bar lab. So, when I moved here, I used my start-up funding to create a similar but more sophisticated setting at the NIH Clinical Center to more closely mimic real-world conditions. NIAAA and the Clinical Center were very receptive to the idea. We test novel medications via human laboratory studies as an important bridge between animal studies and future larger clinical trials. The challenge is to conduct these studies under experimental conditions in a manner that will be useful for work in the real world. The bar lab offers an ecologically valid setting to measure alcohol craving and drinking in a model that resembles a typical and natural environment, while still allowing us to conduct research in a safe and well-controlled manner.

3 Much of your recent work has focused on the hormone ghrelin. How is ghrelin so relevant to the study of AUD?

We know that ghrelin, the “hunger” hormone, plays an important role in appetite and food intake. It is important for survival and stress regulation as well. In the past years, studies in animals and humans, including our own work and that from independent groups, suggest that ghrelin also plays a role in AUD. Our working hypothesis is that we may develop novel effective treatments for AUD by manipulating

the ghrelin system. We are trying to target the ghrelin system using different approaches in our lab and via several exciting collaborative efforts with other NIH labs, universities, and private industry.

Editor’s note: For more information, please see the News From the Field story “Hunger Hormone Affects Alcohol Intake.”

4 Looking ahead a few years, do you see any scientific advances on the horizon?

The use of neuroscience-based approaches to advance our understanding of AUD is increasing, and this is also facilitating cross-talk between scientists and clinicians with different but complementary expertise. For example, there is a significant growth of collaborative work between preclinical and clinical scientists. I am also excited to see a growing number of collaborative efforts between people working in hepatology and neuroscience. Simply, the best way to treat patients with alcoholic liver disease is help them to quit drinking—working together is key to achieve this goal. So, I am optimistic that we will see novel treatments that will help our patients in the not-too-distant future. These treatments may be behavioral, pharmacological, based on brain stimulation techniques, or most likely a combination of these approaches. Chiefly, they will need to be personalized to the individual patient. The key is for all of us to contribute toward a unified and long-term vision. I consider my lab one small piece of a larger puzzle that includes the extraordinary work done by the other NIAAA intramural labs, the NIAAA extramural divisions, and the NIAAA-funded academic centers.

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NEWS FROM THE FIELD: Behavioral Interventions . . . Continued from page 4

The analysis reviewed 21 studies (more than 8,000 participants) that evaluated an individual-level intervention addressing alcohol use either alone or as part of a more comprehensive alcohol/HIV intervention, compared with control conditions that offered no intervention or offered informational content. The analysis also assessed the outcomes of interventions that focused solely on alcohol use versus interventions that focused on alcohol use and other risk behaviors.

The meta-analysis showed that behavioral interventions (e.g., motivational therapy and cognitive behavioral therapy) that addressed alcohol use alone or as one of multiple risk behaviors were effective in reducing alcohol consumption, increasing condom use, and improving HIV medication adherence, relative to control conditions. Additional research is needed to develop, refine, and evaluate interventions to reduce alcohol use and improve health outcomes

among PLWHA, along with additional strategies to integrate alcohol interventions into routine clinical care for PLWHA.

Reference:

Scott-Sheldon, L.A.J.; Carey, K.B.; Johnson, B.T.; Carey, M.P.; and MASH Research Team. Behavioral interventions targeting alcohol use among people living with HIV/AIDS: A systematic review and meta-analysis. *AIDS and Behavior* 21(Suppl. 2): 126–143, 2017. PMID: 28831609

NEWS FROM THE FIELD: Hunger Hormone . . . Continued from page 5

significantly increased the number of alcohol infusions self-administered by the study participants. Participants were also significantly faster to initiate alcohol self-administration when they received ghrelin, compared to placebo.

In another experiment, study participants receiving either intravenous ghrelin or placebo underwent brain imaging. Imaging data showed that ghrelin increased alcohol-related brain activity in the amygdala, a part of

the brain's stress systems implicated in alcohol-drinking behaviors. The hormone also influenced food-related brain activity in the medial orbitofrontal cortex and nucleus accumbens. The

data indicate that ghrelin affects alcohol-seeking behavior in humans and represents a potential new target for AUD medications development.

Reference:

Farokhnia, M.; Grodin, E.N.; Lee, M.R.; Oot, E.N.; Blackburn, A.N.; Stangl, B.L.; Schwandt, M.L.; Farinelli, L.A.; Momenan, R.; Ramchandani, V.A.; and Leggio, L. Exogenous ghrelin administration increases alcohol self-administration and modulates brain functional activity in heavy-drinking alcohol-dependent individuals. *Molecular Psychiatry* November 14, 2017. PMID: 29133954

5 QUESTIONS WITH: Lorenzo Leggio, M.D., Ph.D. . . . Continued from page 7

5 If you didn't pursue a career in medicine and scientific research, what might you be doing now?

I was born in Modica, an ancient Sicilian town famous for its baroque art and delicious food, including a world-famous chocolate inspired by an Aztec recipe. I grew up on a dairy farm managed by my parents and my three brothers, and I worked on the farm

during the summers when I was not at school. But I realized I did not have the talent, cleverness, and passion the rest of my family possesses to be a good farmer. My attention was devoted to reading magazines and books ranging from biology and medicine to literature and humanities. I was living a few miles from Syracuse, where I could see an Aristophanes play in a Greek theater built in fifth-century B.C. I was

intrigued by biomedical science, but I was also in love with the Latin literature, as well as Italian and international humanities. I was struggling, deciding between medical school versus a degree in humanities. In other words, I guess that, if I had not become a physician and scientist, now I would be teaching and studying humanities, possibly living and enjoying the wonderful weather, food, history, and architecture in Sicily.

ABOUT US

NIAAA Spectrum is NIAAA's triannual webzine. With engaging feature articles, short news updates, and colorful graphics, *NIAAA Spectrum* offers accessible and relevant information on NIAAA and the alcohol research field for a wide range of audiences.

Each issue includes feature-length stories, new research findings from the field, image and data analyses, and an interview with an NIAAA staff member or alcohol researcher.

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